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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
LUKTON, DAVID	
ART UNIT	PAPER NUMBER
1654	

DATE MAILED: 03/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/980,624	MARUYAMA ET AL.	
	Examiner	Art Unit	
	David Lukton	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 January 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-6,9-12,14-17 and 19-27* is/are pending in the application.

4a) Of the above claim(s) *2-6,9-12,15-17 and 20-27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14 and 19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Pursuant to the response filed 1/26/05, claims 1, 7, 8, 13, 18, 28 & 29 have been cancelled, and the following claims amended: 2, 4, 9, 10, 14, 17, 19, 20, 23, 24, 26, 27. Claims 2-6, 9-12, 14-17, & 19-27 are now pending.

Pursuant to the restriction and species elections, all claims other than 14 and 19 are withdrawn from consideration. Claims 14 and 19 are examined in this Office action.

Applicants arguments filed 1/26/05 have been considered and found not persuasive.

✦

The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it in such full, clear, concise and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 14 and 19 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 19 asserts that a water-insoluble matrix bearing amino groups or carboxyl groups or sulfate groups can somehow be used to treat sepsis. However, there is

no reason given for why the skilled artisan would believe this to be true. Certainly there is no literature to support such an assertion.

As stated in *Ex parte Forman* (230 USPQ 546, 1986) and *In re Wands* (8 USPQ2d 1400, Fed. Cir., 1988) the factors to consider in evaluating the need (or absence of need) for "undue experimentation" are the following: quantity of experimentation necessary, amount of direction or guidance presented, presence or absence of working examples, nature of the invention, state of the prior art, relative skill of those in that art, predictability or unpredictability of the art, and breadth of the claims. The state of the art is such that the skilled artisan would have expected failure in the treatment of sepsis using, e.g., carboxymethyl sephadex, or diethylaminoethyl sepharose. Given the absence of guidance, the absence of working examples, and the unpredictability of the art, "undue experimentation would be required to practice the invention of claim 19.

Furthermore, even if it is true that e.g., carboxymethyl sephadex, or diethylaminoethyl sepharose or heparin is effective to remove proteins from blood, as applicants have asserted, there are other proteins which would be removed. For example, the following proteins are endogenous to mammals, and at the same time, are anti- inflammatory: interleukin-4, interleukin-10, *alpha*-MSH (melanocyte stimulating hormone), interferon *gamma* binding protein, Il-1 receptor antagonist, and soluble tumor necrosis factor *alpha* receptor.

Removal of any of these is likely to exacerbate the patient's condition. Further, there is also the matter of the rate of HMG-protein removal versus the rate of production. Applicants have not established that they can remove the HMG-protein more rapidly that it is being produced.

Perhaps it is true that some HMG protein can be removed when one of the polymers of claim 19 is used in combination with antibodies to HMG protein. But there is no suggestion or hint in claim 19 that the presence of antibodies is either necessary or desirable. According to applicants' line of reasoning, if a tablet of aspirin together with a glass of water is effective to treat a headache, then water itself is effective to treat a headache. The skilled pharmacologist, however, would take a dim view of such reasoning.

Accordingly, even if it is true that if, for example, dextran sulfate in combination with MAb's to HMG protein is therapeutically effective to treat sepsis (and this point is not conceded), the fact would remain that the claimed adsorbents (*per se*) are not enabled for therapy of sepsis.

It remains the case that "undue experimentation" would be required to practice the claimed invention.

✧

The following is a quotation of the appropriate paragraphs of 35 U.S.C. §102 that form the basis for the rejections under this section made in this action.

A person shall be entitled to a patent unless -

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 14 and 19 are rejected under 35 U.S.C. §102(b) as being anticipated by Petiton (USP 5,378,829).

Petiton discloses sulfated heparin.

The claims encompass sulfated heparin. The properties of absorbing HMG proteins and treating sepsis are inherent.

✦

Claims 14 and 19 are rejected under 35 U.S.C. §102(e) as being anticipated by Aderka (USP 6,608,044).

Aderka discloses not only the existence of heparin, but its use in reducing TNF activity. Also disclosed (col 5, line 42+) is that heparin is sulfated. The claims are anticipated on this basis alone. In addition to the foregoing, it is known in the

art that TNF plays an important role in gram-negative sepsis, and that reducing the levels or activity of TNF is beneficial to patients suffering from such.

Thus, the claims are anticipated.

✧

Claim 19 is rejected under 35 U.S.C. §102(e) as being anticipated by Bell (USP 6,774,102).

Bell discloses a water-insoluble carrier which bears hydrogen-bondable functional groups, and which is useful for therapy of sepsis. Bell does not disclose that the carrier adsorbs HMG proteins, but this property is inherent.

Thus, the claim is anticipated.

✧

The following is a quotation of 35 U.S.C. §103 which forms the basis for all obviousness rejections set forth in the Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.
>
> This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made, absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out the

inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103.

Claims 14 and 19 are rejected under 35 U.S.C. §103 as being unpatentable over Stuber (USP 5,116,962).

As indicated previously, Stuber discloses an adsorbent bearing sulfate groups. Stuber does not disclose that the adsorbent will adsorb HMG proteins. However, the chromatographic specialist (of ordinary skill) would have expected that if the pH of the eluting buffer is below the isoelectric point (IEP) of a given protein, there will be at least some adsorption. That is, if one were to take a given protein "X" which has an IEP of "Y", and load that protein "X" onto a sulfated chromatographic matrix, the result would be that protein "X" would elute after the void volume if the pH of the buffer were less than the IEP.

In response, applicants have argued that the reference does not employ the phrase "hydrogen bondable functional group". However, there is no court case or statute which holds that in order for a §103 or §102 rejection to be proper, the language used in the reference must be the same as the language recited in the claims. What is true, and applicants' counsel may be aware of this, is that in rejecting a claimed genus over a reference, it is quite sufficient that the reference disclose just one member of that genus. This situation is, in fact, more the rule than the exception. Thus, while it may be true that the reference does not employ

the phrase "hydrogen bondable functional group", it is nevertheless true that the reference discloses at least one member of the genus. Adsorbents bearing sulfate groups, as it happens, are those that are most preferred by applicants.

Applicants have also argued that the particular adsorbents disclosed in the reference will not adsorb HMG proteins. However, applicants have provided no evidence, or even reasoning as to why this might be true. In fact, applicants have not even asserted that the Stuber adsorbents will not bind HMG proteins. The fact is that it is applicants who have argued, via the specification, that if an adsorbent bears sulfate groups, it will bind HMG proteins. If applicants are now having doubts about that, applicants should convey the same. At least, if applicants feel confident that the sulfate-bearing adsorbents (of the Stuber patent) cannot be made to bind HMG proteins, then applicants should assert this, and provide at least some reasoning as to why this might be true. In the absence of this, it will remain clear that applicants have no conviction in their view that this ground of rejection is improper.

The rejection is maintained.

✦

Claim 19 is rejected under 35 U.S.C. §103 as being unpatentable over Abbot (USP 4,430,496).

Abbot discloses an adsorbent bearing trimethylammonium groups. Abbot does not disclose that the adsorbent will adsorb HMG proteins. However, the chromatographic specialist (of ordinary skill) would have expected that if the pH of the eluting buffer is above the isoelectric point (IEP) of a given protein, there will be at least some adsorption. That is, if one were to take a given protein "X" which has an IEP of "Y", and load that protein "X" onto a cationic chromatographic matrix, the result would be that protein "X" would elute after the void volume if the pH of the buffer were above the IEP of the protein.

In response, applicants have argued that quaternary ammonium groups have no capacity to bind hydrogen ions. However, even if this is true, it is applicants who have clearly asserted that this is the case. Applicants are requested to consider claims 3-6 of the instant specification, as well as relevant passages in the description of the invention. If applicants now believe that claims 3-6 describe an invention which is distinct from that of claim 19, it is suggested that applicants do both of the following: (a) make a clear, unequivocal admission that claims 3-6 describe an invention which is distinct from that of claim 19, and (b) cast claim 3 in independent form. If both of these are done, the rejection may be reconsidered. Better still would be to amend claim 19 to specifically exclude cationic functional groups.

Applicants have also argued that "the pH of the column cannot be altered". However, nowhere in the language of claim 19 is there any suggestion that a column might be necessary or desirable. Applicants have also argued that the claims impose some sort of limitation on the pH of blood. Again, applicants are not correct. There is no mention anywhere of either blood or pH in the rejected claim.

Applicants have also argued that Abbot '496 does not teach that the disclosed trimethylammonium group-bearing adsorbents will bind HMG protein. In response, the arguments presented above (the §103 over Stuber '962) apply here as well.

The rejection is maintained.

✦

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Lukton whose telephone number is 571-272-0952. The examiner can normally be reached Monday-Friday from 9:30 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell, can be reached at (571)272-0974. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

DAVID LUKTON, PH.D.
PRIMARY EXAMINER